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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/845,612 | 04/30/2001 | Hongtao Yu | UTSD:795US | 2625 |

7590 12/23/2003
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EXAMINER

HUFF, SHEELA JITENDRA

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1642

DATE MAILED: 12/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/845,612

Applicant(s)

YU ET AL.

Examiner

Sheela J Huff

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 39-45 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 39-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

Response to Amendment

The amendment filed on 11/3/03 has been considered.

Claims 39-45 are pending.

The previous rejection is withdrawn in favor of a new one.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 39-45 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well established utility.

Applicant discloses and claims a screening assay which screens for compounds that (1) inhibit the biochemical function of Mad2 and (2) further screening the compounds found to effective in (1) for anti-cancer effects. In support of this applicant shows a consensus peptide sequence that interacts with Mad2 and that it can block the biochemical function of Mad2. However, the claimed invention calls for not only determining which compounds bind to Mad2 and block function but also calls for screening that compound for anti-cancer effects.

With respect to Mad2 and its connection to cancer, the state of the art merely states that Mad2 "is expressed at lower levels in breast cancer cell line T47D as compared to normal cells (Li et al, 1996)" (page 3, lines 21-22 of the specification). A close review of Li et al shows that the reference concludes that "defects in the mitotic checkpoint **may contribute** to the sensitivity of certain tumors to mitotic spindle

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inhibitors”(emphasis added, last line of abstract). Furthermore, on page 248, second column the reference discloses that two different taxol/nocodazole sensitive cells lines (T47D (breast cancer) and RH1 (rhabdomyosarcoma) failed to under mitotic arrest and that only the T47D cell line showed a decrease in MAD2. Thus, it appears that the state of art may only recognize the connection of Mad2 with possibly only one type of cancer (breast). Thus, in view of Li et al it is not clear if MAD2 is definitively linked to breast cancer and it is clear that MAD2 is not linked to all types of cancer.

Applicant's examples do show that the invention has utility. Applicant has shown that peptides that bind to the cdc20 domain of Mad2 can block the biochemical function of MAD2 in vitro. Applicant provides no examples to show that these peptides have any anti-cancer effects. In fact, on page 4 of the response filed 11/3/03 applicant clearly support this lack of evidence by stating “[A]pplicant's acknowledge that no Mad-binding has been examined for *in vivo* effects on cancer cells”(second line from the bottom of the page). Thus, since there is no objective credible evidence to show that Mad is linked to breast cancer and since applicant's have not provided any evidence to refute this, the Examiner believes that the claimed invention does not meet the utility requirement.

Claims 39-45 are also rejected under 35 U.S.C. 112, first paragraph.

Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 39-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

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described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described in *In Re Colianni*, 195 USPQ 150 (CCPA 1977) and have been adopted by the Board of Patent Appeals and Interferences in *Ex Parte Forman*, 230 USPQ 546 (BPAI 1986). Among these factors are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the breadth of the claims,
5. the amount of direction or guidance present, and
6. the presence or absence of working examples.

The following is an analysis of these factors in relationship to this application.

Nature of the invention

Applicant discloses and claims a screening assay which screens for compounds that (1) inhibit the biochemical function of Mad2 and (2) further screening the compounds found to effective in (1) for anti-cancer effects.

State of the Art/Predictability

With respect to Mad2 and its connection to cancer, the state of the art merely states that Mad2 "is expressed at lower levels in breast cancer cell line T47D as compared to normal cells (Li et al, 1996)" (page 3, lines 21-22 of the specification). A close review of Li et al shows that the reference concludes that "defects in the mitotic checkpoint **may contribute** to the sensitivity of certain tumors to mitotic spindle inhibitors"(emphasis added, last line of abstract). Furthermore, on page 248, second column the reference discloses that two different taxol/nocodazole sensitive cells lines (T47D (breast cancer) and RH1 (rhabdomyosarcoma) failed to under mitotic arrest and that only the T47D cell line showed a decrease in MAD2. Thus, it appears that the

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state of art may only recognize the connection of Mad2 with possibly only one type of cancer (breast). Thus, in view of Li et al it is not clear if MAD2 is definitively linked to breast cancer and it is clear that MAD2 is not linked to all types of cancer.

Guidance/Working Examples

Applicant has not provided any working examples to show that peptides which block the biochemical function of MAD2 possess the ability to produce anti-cancer effects. In fact, on page 4 of the response filed 11/3/03 applicant clearly supports this lack of evidence by stating "[A]pplicant's acknowledge that no Mad-binding has been examined for *in vivo* effects on cancer cells"(second line from the bottom of the page).

Breadth of the claims

Even if applicant can show a clear link between MAD2 and breast cancer, applicant is clearly claiming very broadly. Applicant claims that the screened compound would be effective in any type of cancer. The claimed invention reads on all types of cancers, including, but not limited to prostate cancer, lung cancer, brain cancer, pancreatic cancer and liver cancer (see paragraph bridging page 4-5 of the specification for a more extensive list of cancers). As shown by Li et al (discussed above), the only possible connection that MAD2 has to cancer is to breast cancer. The reference also shows that there is no connection between rhabdomyosarcoma and MAD2. In view of this, it is the Examiner's position that applicant is claiming very broadly.

In view of the above, it is the Examiner's position that one skilled in the art could not make and/or use the invention without undue experimentation.

Response to Applicant's arguments to the extent that they pertain to the above rejection

Applicant argues that the "knowing what compounds **do not** bind and/or inhibit is

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valuable information" (page 4, middle). This is an assertion and applicant has not provided any objective evidence to show the value of the compounds. Applicant further refers to page 22 of the specification. This page merely re-interates applicant's assertion.

Claims 39-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The preamble of the claim is vague and unclear because it does not state what the screening method of screening for.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J Huff whose telephone number is 703-305-7866. The examiner can normally be reached on Tuesday 5:30am-11:30am and Fridays 6:00am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.


Sheela J Huff

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Primary Examiner
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sjh